TABLE 1.—*Criteria for Determining the Need for Preventive Therapy*

Category	*Age < 35 Years*	*Age ≥ 35 Years*
No risk factor, low-incidence group	Treat if PPD ≥ 15 mm	Do not treat
No risk factor, high-incidence group†	Treat if PPD ≥ 10 mm	Do not treat
Risk factor* present, either incidence group	Treat all ages if PPD ≥ 5 mm and has HIV infection, recent contact with infectious person, or fibrotic lesions on chest radiograph	
	Treat all ages if PPD ≥ 10 mm and there is recent tuberculin skin test conversion (≥ 10 mm increase for those younger than 35; ≥ 15 mm increase for those 35 years and older); intravenous drug use; or patient has medical conditions that may increase risk of tuberculosis	

*Risk factors include HIV infection, recent contact with infectious person, fibrotic lesion on chest radiograph, recent tuberculin skin test conversion, intravenous drug use, or the presence of medical conditions that may increase the risk of tuberculosis, such as diabetes mellitus, silicosis, immunosuppression, or malnutrition.

†High-incidence group includes foreign-born persons from high-prevalence countries, African Americans, Hispanics, Native Americans, and residents of long-term-care facilities and correctional institutions.

munodeficiency virus (HIV); and elderly residents of long-term-care facilities.

The best way to identify persons infected with tubercle bacilli is the intradermal purified protein derivative (PPD) skin test. The tuberculin skin test is one of the oldest medical technologies still in daily use. Tuberculin was first derived by Koch in 1890; Mantoux, a French physician, developed the intradermal skin test in 1908; and purified protein derivative of tuberculin was first produced in 1934. Despite 50 years of research, there still is no better screening test for determining who has been infected and, therefore, who is at risk for active tuberculosis developing.

Unfortunately, the cross reactivity of the skin test with nontuberculous mycobacterial exposure frequently results in positive tests in those who come from areas of high nontuberculous mycobacterial prevalence—such as southern United States—or in those who have had a bacille Calmette Guérin (BCG) vaccination, which is still used in many Asian and Central and South American countries. The size of this reaction is usually from 10 to 15 mm of induration but may be boosted by repeated testing. On the other hand, using 10 mm as a cutoff point may give false-negative interpretations in situations where it is important to offer preventive therapy—such as those recently infected or who are HIV-positive.

These factors have prompted the Centers for Disease Control's (CDC's) Advisory Committee for the Elimination of Tuberculosis to change the criteria for recommending isoniazid preventive therapy. These new criteria, based on age, incidence, and risk factors, are given in Table 1.

The two key changes are the recommendation that a PPD result of 5 mm or more of induration is a positive test in populations with risk factors for *Mycobacterium tuberculosis* infection and that a PPD reaction must be 15 mm or more to be interpreted as positive in those at low risk. This latter change is to avoid false-positive interpretations and to minimize potentially inappropriate preventive therapy.

Regardless of the CDC's criteria changes, isoniazid preventive therapy (300 mg per day for 6 to 12 months) works. It will prevent the development of active tuberculosis in those infected, both while they take it and for many years (if not a lifetime) thereafter. The widespread and continued use of preventive therapy is our best hope of again decreasing the number of persons with active tuberculosis in the United States.

JONATHAN E. RODNICK, MD
San Francisco, California

REFERENCES

American Thoracic Society: The tuberculin skin test. Am Rev Respir Dis 1981; 124:356-363

Bass JB, Sanders RV, Kirkpatrick MB: Choosing an appropriate cutting point for conversion in annual tuberculin skin testing. Am Rev Respir Dis 1985; 132:379-381

Centers for Disease Control: The use of preventive therapy for tuberculosis infection in the United States: Advisory Committee for Elimination of Tuberculosis. MMWR 1990; 39(RR-8):9-12

De March-Ayuela P: Choosing an appropriate criterion for true or false conversion in serial tuberculin testing. Am Rev Respir Dis 1990; 141(Pt 1):815-820

Zidovudine in the Treatment of Human Immunodeficiency Virus Disease

THE TREATMENT of human immunodeficiency virus (HIV) disease initially consisted of antimicrobial therapy for the opportunistic infections associated with the acquired immunodeficiency syndrome (AIDS). More recent research has been directed at developing a means of controlling the progression of infection by the virus itself. Zidovudine (AZT) is a thymidine analogue that inhibits HIV viral replication by interfering with the function of the viral reverse transcriptase.

Researchers reported the results of a placebo-controlled trial of zidovudine in adults with AIDS or severe AIDS-related complex. At a dose of 1,500 mg of zidovudine per day, there was a statistically significant decrease in mortality and the frequency of severe opportunistic infections that persisted for 18 months. Hematologic side effects were seen and included severe anemia and neutropenia.

The recent AIDS Clinical Trial Group Study examined the use of zidovudine in asymptomatic adults infected with HIV who had a CD4 cell count below 0.5×10^9 per liter (500 per μl). People were assigned to one of three treatment groups: those receiving placebo, 500 mg of zidovudine per day, or 1,500 mg of zidovudine per day. There was significantly less progression to AIDS or advanced AIDS-related complex in the two zidovudine treatment groups compared with the placebo group. There was no advantage to the higher dose of zidovudine in preventing the progression of HIV disease. The high-dose zidovudine group had the known hematologic side effects of anemia and neutropenia. These were not seen in the low-dose or placebo groups. The only side effect that was unique to the low-dose zidovudine group was nausea. The use of zidovudine in HIV-infected persons with CD4 counts greater than 0.5×10^9 per liter is under investigation.

These are important clinical findings in light of the fact

that most HIV-infected persons are currently asymptomatic. Primary care providers are in a position to identify persons who may benefit from the prophylactic use of zidovudine by offering HIV testing to their patients. The Food and Drug Administration has recently approved the use of zidovudine therapy (500 mg per day in five 100-mg doses) in persons with CD4 cell counts below 0.5×10^9 per liter. Patients receiving 500 mg per day of zidovudine should be monitored monthly with complete blood counts. Hemoglobin levels of less than 4.96 mmol per liter (8 grams per dl) or neutropenia, or both, indicate serious hematologic complications and may require discontinuation of the medication or a reduction in medication dose.

Questions remain regarding the long-term use of prophylactic zidovudine. The long-term side effects, the impact on survival, and the clinical significance of possible drug resistance are not known. Despite these uncertainties and the relatively high cost of zidovudine therapy, the minimal side effects with a 500-mg-per-day dose and the apparent delay in disease progression to AIDS make the use of zidovudine prophylaxis a serious consideration for asymptomatic HIV-infected persons with CD4 lymphocyte counts below 0.5×10^9 per liter.

MARIANNE A. McKENNETT, MD
San Diego, California

REFERENCES

AZT therapy for early HIV infections. AIDS Clinical Care 1990; 2:37-38. Adapted from the Executive Summary of the State-of-the-Art Conference on AZT Therapy for Early HIV Infection. Sponsored by the National Institute of Allergy and Infectious Diseases, March 1990

Fischl MA, Richman DD, Grieco MH, et al: The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex: A double-blind, placebo-controlled trial. N Engl J Med 1987; 317:185-191

Volberding PA, Lagakos SW, Koch MA, et al: Zidovudine in asymptomatic human immunodeficiency virus infection: A controlled trial in persons with fewer than 500 CD4-positive cells per cubic millimeter—The AIDS Clinical Trials Group of the National Institute of Allergy and Infectious Diseases. N Engl J Med 1990; 322:941-949

Advances of the United States Preventive Services Task Force in Health Promotion and Disease Prevention

HEALTH PROMOTION and disease prevention are important aspects of family practice. Over the years, many opinions and recommended guidelines have been promulgated, but it has always been left up to individual practitioners to decide which interventions to use. In 1984 the US Department of Health and Human Services convened a special working group, the US Preventive Services Task Force. This group worked collaboratively with the Canadian Task Force on the Periodic Health Examination, which had previously done extensive work in the area. The result of this collaborative effort is the first set of truly comprehensive guidelines on the subject: the *Report of the US Preventive Services Task Force: Guide to Clinical Preventive Services.*

This guide synthesizes four years of extensive review of existing medical literature and interviews with numerous experts on preventive services. It contains recommendations on 169 screening, counseling, and immunization interventions for the prevention of 60 different common illnesses and conditions. Among the topics covered are cholesterol, coronary artery disease, breast and other cancers, prenatal disorders, nutrition, low back injury, dental disease, childhood and adult immunizations, chemoprophylaxis after exposure to various infections, smoking, alcohol abuse, and motor vehicle injuries.

The scientific basis for each intervention is evaluated in the following areas: "burden of suffering" (incidence, prevalence, morbidity, and mortality); "efficacy of screening tests" (sensitivity, specificity, predictive value, and reproducibility); and "effectiveness of early detection" (availability of "clinical interventions which can prevent or delay progression of the disorder"). For example, in the area of colorectal cancer, the task force neither endorses nor discourages screening, noting that despite the high burden of suffering, the efficacy of available screening methods is suboptimal and the effectiveness of early detection is not conclusively proved. It recommends screening for high-risk persons.

In other controversial areas, the task force also takes a middle-of-the-road position. In contrast to the 1988 recommendations of the National Cholesterol Education Program Expert Panel in which cholesterol screening is recommended every five years for all adults older than 20 years, the task force's recommendation is for "periodic screening" of middle-aged men. The task force mentions the expert panel's recommended frequency of every five years and states that it may be "clinically prudent" to screen others as well. The task force's "suggested threshold" for drug therapy is higher than the 1988 panel's recommendations, namely, a cholesterol level of 6.21 mmol per liter (240 mg per dl) in high-risk patients and 6.85 mmol per liter (265 mg per dl) in patients with no risk factors, versus 5.17 mmol per liter (200 mg per dl) and 6.21 mmol per liter, respectively. The task force's reasoning is that the effect on coronary artery disease of drug therapy in persons other than middle-aged men with levels of 6.60 to 6.85 mmol per liter (255 to 265 mg per dl) has not yet been proved; therefore, the potential risks and costs are not justified.

In the area of breast cancer screening, the task force's recommendations are also slightly different from previously published guidelines. In contrast to the 1987 and 1988 recommendations of the American Cancer Society and the National Cancer Institute, the task force recommends annual breast examination for all women beginning at age 40 and mammography every one to two years beginning at age 50. The recommendation for Pap testing is similar to the 1988 consensus statement adopted by the American Cancer Society, the American Academy of Family Physicians, and others, except for the addition of a recommended discontinuation at age 65 in women with previously normal Pap smears.

The recommended use of all of the interventions is summarized in a series of tables grouped according to age, sex, and other risk factors. Each table is appended with footnotes that detail the high-risk conditions for which certain interventions should be applied. Also listed in each table are the leading causes of death for each group, such as motor vehicle crashes, homicide, and suicide in teenagers; additional preventive services to be considered; and items to "remain alert for"—such as depression, abuse and neglect, and dental disease in the elderly.

Several important conclusions and implications emerged from the task force's review of existing evidence. First is that the most important contributors to preventable morbidity and mortality are the personal health behaviors of smoking, alcohol use, poor nutrition, and physical inactivity. The implication of this is that interventions which address these behaviors, namely counseling and patient education, may have a more valuable effect than the conventional ordering of tests. Further, as the locus of responsibility for personal health